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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/711,619	11/13/2000	Gurmukh S. Johal	35718/205458	7883

29122 7590 11/04/2002

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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/04/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/711,619	JOHAL ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 20-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

STATUS OF THE APPLICATION

Priority

1. Applicant's statement filed 21 August 2002 has been noted by the Examiner (page 10 of the Remarks).

Response to Objections and Rejections

2. Claims 19 and 25-32 have been cancelled without prejudice.

3. The objection to claims 1, 4, 10 and 24 are withdrawn in view of Applicant's amendments to the claims, the objection to claim 19 is now moot because said claim has been cancelled.

4. The rejection of claims 4-17 and 20-24 under 35 U.S.C. § 101 because the claimed invention appears to be inoperable and thus lacks patentable utility is withdrawn in view of Applicant's amendments to the claims and Applicant's arguments.

5. The rejection of claims 1-24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendments to the claims, claim 19 has been cancelled.

6. The rejection of claim 1 under 35 U.S.C. § 102(b) as being anticipated by Dudler *et al* 1992 (The Journal of Biological Chemistry) is withdrawn in view of Applicant's amendment to the claim.

7. The rejection of claim 1 under 35 U.S.C. § 102(b) as being anticipated by Wang *et al* 1996 (Plant Molecular Biology 31:683-687) is withdrawn in vie of Applicant's amendment to the claim.

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

9. Claims 1-18 and 20-24 remain rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 21 May 2002. Applicant's arguments filed 21 August 2002 have been fully considered but they are not persuasive.

Applicant argues that the recitation of at least 80% sequence identity to the sequence set forth in SEQ ID NO 7 or 8 is a very predictable structure of the sequences encompassed by the claimed invention in addition to nucleotide sequences obtained by hybridization under the claimed stringent conditions (page 14, last paragraph of the Remarks). Applicant also argues that knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention (page 15, first paragraph of the Remarks). This argument is not found to be persuasive because Applicant does not describe other nucleotide molecules encoding a non-mutant P-glycoprotein that controls plant growth other than that of SEQ ID NO: 7 or 8, or a nucleotide molecule that encodes the amino acid sequence of SEQ ID NO: 9. Such a description would also be required to envision a nucleic acid that would bind under the claimed stringency conditions. In addition, because SEQ ID NO: 7 is the genomic sequence for the cDNA

exemplified in SEQ ID NO: 8, hence Applicant has only described a single nucleotide molecule that encodes the P-glycoprotein of SEQ ID NO: 9.

Applicant argues that Applicant may also rely upon functional characteristic in the description, provided there is a correlation between the function and structure of the claimed invention, specifically, sequences encoding P-glycoproteins that function to control plant growth (page 15, 3rd paragraph of the Remarks). This argument is not found to be fully persuasive. See, MPEP § 2163 which states that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. In the instant case, Applicant has not described what structural characteristics, within the claimed 80% limitation, that are correlated with the function of the claimed nucleotide molecule, and thus has not adequately describe the claimed genus of nucleotide molecules that encode P-glycoproteins that function to control plant growth.

10. Claims 18 and 20-23 remain rejected and claims 1-17 and 24 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method for modifying the height of a sorghum plant comprising transforming said sorghum plant with a construct comprising a nucleotide molecule having the nucleotide

sequence of SEQ ID NO: 7 or 8 in either the sense or antisense configuration, does not reasonably provide enablement for a method of modifying the growth of any organism or specifically a plant comprising transforming said organism with any nucleotide molecule encoding a p-glycoprotein that functions to control growth of an organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is repeated for the reason of record as set forth in the last Office action mailed 21 May 2002. Applicant's arguments filed 21 August 2002 have been fully considered but they are not persuasive. This rejection has been modified to include claims 1-17 and 24. Those issues affecting the additionally rejected claims will be addressed below.

Applicant has provided limited guidance for those critical features of a P-glycoprotein that are required to modify the growth of a transformed plant as claimed. The art teaches that it cannot be predicted by one of skill in the art that nucleic acids that are 80% identical will encode a protein with the same activity as that exemplified by Applicant in SEQ ID NO: 9. Bowie *et al* (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie *et al* teach that while

it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column).

The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar *et al* (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract). Small changes in amino acid sequence can completely modify enzymatic function; Broun *et al* (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Lazar *et al* and Broun *et al* demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm.

244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein. The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

As to the limitation of a nucleotide sequence that hybridizes under the claimed stringent conditions, the art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe or sequence of interest. Fourgoux-Nicol *et al* (1999, Plant Molecular Biology 40: 857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65° C (page 859, left column, 2nd paragraph). Fourgoux-Nicol *et al* also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could

hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe.

Applicant argues that the specification provides sufficient guidance to make and identify the nucleotide molecules encompassed by the claims and that the nucleotide molecules of the invention encode P-glycoproteins that are capable of controlling the growth of an organism, particularly plants (last paragraph on page 17 and first paragraph on page 18 of the Remarks).

This argument is not found to be persuasive because the functional limitation in the claims does not teach one of skill in the art how to make and use the invention as broadly claimed. Applicant has only provided guidance for isolating and using a nucleotide molecule encoding the sorghum P-glycoprotein exemplified in SEQ ID NO: 9. The examples for modifying the growth of a heterologous plant, such as maize, using the isolated nucleotide molecule appears prophetic and does not provide any guidance to one of skill in the art as to how to make and use the invention within the breadth of the claims (see Examples 3 and 4 on pages 48-51 of the specification).

Applicant agues that the claimed methods involve the expression of the nucleotide molecules in either the sense or antisense orientation and do not depend on use in a particular plant species such as sorghum (page 17, 3rd paragraph of the Remarks). The Examiner responds that this argument does not address the rejection concerning the scope of enablement for a method of modifying the growth of any plant, nor does this argument address the issue of how one of skill in the art would use such any plant as encompassed by newly rejected claims 4-17 and 24.

Applicant argues that the quantity of experimentation required to practice the invention amounts to two steps, generating a nucleotide sequence having at least 80% sequence identity to SEQ ID NO: 7 and/or 8, or hybridizing under stringent conditions to SEQ ID NO: 7 and/or 8, and assaying for functional activity (page 19, 2nd paragraph of the Remarks). This argument is not found to be persuasive, because as pointed out by the teachings of the art above, by only changing a few codons encoding different amino acids in a nucleotide molecule one can substantially change the functional properties of an encoded protein, hence without substantial guidance by Applicant as to what encoded amino acid sequences are required to practice the invention within the scope of the claims, it would have required undue trial and error experimentation by one of skill in the art at the time of Applicant's invention to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

11. Claims 1-6, 9, 11-13, 16, 18, 20, 21 and 24 remain rejected under 35 U.S.C. § 102(b) as anticipated by Sidler *et al* 1998 (The Plant Cell 10:1623-1636). This rejection has been modified from that in the last Office action mailed 21 May 2002. This rejection is repeated for the reason of record as set forth in the last Office action mailed 21 May 2002. Applicant's arguments filed 21 August 2002 have been fully considered but they are not persuasive.

Sidler discloses an isolated nucleotide molecule that would hybridize under the claimed stringency conditions to SEQ ID NO: 7 or 8 (see page 1633, left column, second paragraph). Sidler discloses complementary sequences of said isolated

nucleotide molecule, an expression cassette comprising said sense or antisense nucleotide molecule operable linked to a constitutive promoter and plants transformed with said cassette. Sidler discloses that the native promoter of the AtPGP1 gene is a tissue-preferred promoter (see page 1626-1627). Sidler discloses that the isolated nucleotide molecule encodes a P-glycoprotein that functions to control the growth of an organism (see pages 1633-1634, and page 1623). Sidler discloses a method of modifying the growth of a plant comprising transforming a plant with an antisense construct operably linked to a constitutive promoter that produces an antisense transcript that modifies the growth of a plant, specifically *Arabidopsis thaliana* (see the abstract on page 1623). Sidler also discloses a method of modifying the growth of a plant comprising transforming a plant with a sense construct, leading to the production of longer roots due to overexpression of the gene product (see page 1626). The transformed monocot plants at claims 7, 8, 14, 15, 22 and 23 would have been considered functional equivalents to the *Arabidopsis thaliana* plant of Sidler. Hence, Sidler has previously disclosed all of the claim limitations.

Applicant argues that claims 1, 4, 18 and 24 have been amended to recite specific stringent conditions and thus Sidler does not disclose the claimed invention (paragraph spanning page 21 of the Remarks). This argument is not found to be persuasive. The Examiner notes that there is no recitation of washing time(s) in the instant claims, and that the recited wash conditions are only of low to moderate stringency. Given the evidence of Fourgoux-Nicol *et al* (1999, Plant Molecular Biology

40: 857-872) discussed above, the instant claims appear to remain anticipated by Sidler *et al.*

Claim Rejections - 35 USC § 103

12. Claims 7, 9, 10, 14, 15, 17, 22 and 23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sidler *et al* 1998 (The Plant Cell 10:1623-1636), in view of Applicant's admission.

The teachings of Sidler are discussed supra.

Sidler does not teach transformation of monocot plants or transformation of dicot plants other than *Arabidopsis.*

Applicant admits that methods of transforming monocot plants, such as maize and rice, and dicot plants, such as soybean, were known in the art at the time of Applicant's invention (see paragraph spanning pages 34-35 of the specification).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Sidler to transform plants other than *Arabidopsis thaliana* with the AtPGP1 gene using transformation method known in the art at the time of Applicant's invention. The success of Sidler in modifying the growth of *Arabidopsis thaliana* by overexpressing the AtPGP1 gene would have motivated one of ordinary skill in the art to transform other plants with said gene and would have given on of ordinary skill a reasonable expectation of success.

Double Patenting

13. Claims 1-18 and 20-24 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-18, 20-22 and 29 of copending Application No. 09/711,562. Applicant does not specifically address this rejection in the response filed 23 August 2002. The Examiner would additionally like to direct Applicant's attention to page 47, lines 14-27, which disclose that the maize Br2 gene and the sorghum Dw3 gene are 92% identical at the nucleotide level.

Conclusion

14. No claims are allowed.

15. This Office Action is non-final.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Amy Nelson

David H. Kruse, Ph.D.
24 October 2002

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